## REMARKS

The Office Action dated May 5, 2005, has been received and carefully noted. The amendments made herein and the following remarks are submitted as a full and complete response thereto.

Claims 1-3, 5, 7-11, 13, 14, 16, as well as the specification have been amended. In addition, an Abstract on a separate page has been submitted for consideration. The Applicants respectfully submit that the amendments made here are fully supported in the disclosure of the present application as originally filed, and therefore no new matter has been added. Accordingly, claims 1-17 are pending in the present application and are respectfully submitted for consideration.

**Claim Objection**

Claim 5 was objected to for having improper periods. Claim 5 has been amended to obviate this objection, and therefore is in compliance with U.S. patent practice. The Applicants respectfully request withdrawal of the objection.

**Abstract**

The Applicants thank the Examiner for highlighting the missing Abstract from the present application. An Abstract of the present invention is submitted herewith on a separate sheet for consideration.

**Specification**

The specification has been amended. In particular, the "Cross-Reference to Related Applications" section of the application has been amended and updated with

the status of each U.S patent application. Accordingly, The Applicants respectfully submit that the present application is in compliance.

**Rejection Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-17 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-3, 5, 7-11, 13, 14, and 16 have been amended to more clear recite the subject matter of the present invention, and to obviate the rejection.

The Applicants respectfully submit that claims 1 and 5 have been amended to more clearly recite a list of interconnected elements. Specifically, the elements in lines 14-20 are more clearly recited such that they are more interconnected to the elements recited in lines 3-13. Claim 5 has been similarly amended along these lines.

For example, the subject matter of "said test sample" recited in line 15 of claim 1 is interconnected to the "plurality of test samples" from "a primary compound library" recited in lines 3-4.

In addition, the Applicants have amended the phrase "selecting a predetermined absorption profile" to --selecting a desired *in vivo* absorption profile--. The Applicants note that the term "desired" is not a vague or indefinite term since it is, for example a variable element of the claim that can be supported at least on page 23, lines 11-28. For instance, the parameters of the "desired *in vivo* absorption profile" can be ascertained by at least the above highlighted section of the present disclosure, and thus is not indefinite.

As for the issues raised with respect to claims 7, 8, 11, 9-11, 13 and 14, the Applicants submit that the claims have been amended to obviate the rejection.

Regarding the issue raised with respect to claim 15 concerning the phrase "said physiological model" recited in line 1, the Applicants respectfully traverse and submit that the antecedent basis for said phrase appears in claim 5 and in claim 2, for which claim 15 depends.

In particular, claim 15 depends from claim 2 or 6. Claim 6 depends from claim 5, and claim 5 recites "a physiological model" in line 18. Moreover, claim 2 recites "a physiological model" in line 6. Accordingly, it is submitted that the phrase "said physiological model" recited in claim 15 does indeed have proper antecedent basis.

In view of the above, the Applicants respectfully requested that the rejection be withdrawn.

**Rejection Under 35 U.S.C. § 112, First Paragraph**

Claims 1-17 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claims 1-3, 5, 7-11, 13, 14, and 16 have been amended to obviate the rejection.

The Applicants respectfully highlight at least page 15, lines 10-25; page 16, lines 15-30; as well as page 23, lines 11-28 of the present specification, which clearly support the subject matter recited in the claims.

For instance, page 15, lines 19-20 disclose "selecting test samples having a desired absorption profile..." Also, page 16, lines 16-19 disclose "...method for generating an in vivo absorption profile is by providing initial dose and in vitro bioavailability data for each test sample..." for example. Moreover, the Applicants refer to page 23, lines 11-15, which discloses "a second compound library" for example.

Accordingly, the Applicants respectfully request that the rejection be withdrawn.

**Rejection Under 35 U.S.C. § 102**

Claims 1-3, 5-10, 12, 13, 15 and 16 are rejected under 35 U.S.C. § 102(a) as being anticipated by Wessel et al. (Publication entitled "Prediction of human intestinal absorption of drug compounds from molecular structure," J. Chem Inf Computer Science, July-August 1998, hereinafter "Wessel"). To the extent that this rejection remains applicable to the claims as amended, the Applicants respectfully traverse the rejection and submit that each of these claims recites subject matter that is neither disclosed nor suggested by the cited prior art.

Amended claim 1 recites,

> A method of screening a compound library or portion thereof by absorption, said method comprising:
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> providing a primary compound library or portion thereof having a plurality of test samples containing isolated compounds or isolated mixtures of compounds per test sample;
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> generating *in vitro* bioavailability data from each of said test samples, the bioavailability data comprising permeability and solubility data;
>
> generating an *in vivo* absorption profile for each of said test samples from initial dose data and from the generated *in vitro* bioavailability data, wherein said *in vivo* absorption profile is characterized by one or more of rate of absorption, extent of absorption, and concentration of a test sample relative to a selected site of administration and a selected sampling site for one or more physiological barriers to absorption of a mammalian system of interest;
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> selecting a desired *in vivo* absorption profile;

screening said test samples from said primary compound library for *in vivo* absorption profiles that are above or equivalent to the desired *in vivo* absorption profile; and

generating a secondary compound library from said screening of said test samples.

Amended claim 5 recites,

A method of screening a compound library or portion thereof by absorption, said method comprising:

providing a primary compound library or portion thereof having a plurality of test samples containing isolated compounds or isolated mixtures of compounds per test sample;

generating *in vitro* bioavailability data from each of said test samples, the bioavailability data comprising permeability and solubility data;

generating a simulated *in* vivo absorption profile for each of said test samples from initial dose data and from *in vitro* bioavailability data, wherein said absorption profile is characterized by one or more of rate of absorption, extent of absorption, and concentration of a test sample relative to a selected site of administration and a selected sampling site for one or more physiological barriers to absorption of a mammalian system of interest, wherein said simulated *in vitro* absorption profile is generated by:

providing said initial dose data and said *in vitro* bioavailability data to a computer–implemented pharmacokinetic tool (PK tool) which comprises a s computer-readable components, an input/output system, a simulation engine, and a simulation model comprising a physiological model of said mammalian system of interest, wherein said input/output system, simulation engine and simulation model are capable of working together to carry out the steps of:

receiving through the input/output system as input data, said initial dose data and said *in vitro* bioavailability data for one or said test samples; and

generating as output data a simulated *in vivo* absorption profile for said test samples;

selecting a desired simulated *in* vivo absorption profile;

screening said test samples from said primary compound library for simulated *in vivo* absorption profiles that are above or equivalent to the desired simulated *in vivo* absorption profile; and

generating a secondary library from said screening of said test samples.

Wessel merely discloses a data set of 86 drug and drug-like compounds with measured values of %HIA taken from the literature, and was used to develop and test a QSPR mode. The compounds were encoded with calculated molecular structure descriptors. Furthermore, Wessel only provides that a nonlinear computational neural network model was developed by using the genetic algorithm with a neural network fitness evaluator. The calculated %HIA (cHIA) model performs well, with root-mean-square (rms) errors of 9.4%HIA units for the training set, 19.7%HIA units for the cross-validation (CV) set, and 16.0%HIA units for the external prediction set.

The Applicants submit that Wessel fails to disclose or suggest each and every element recited in amended claims 1 and 5 of the present application. In particular, it is submitted that the prediction of human intestinal absorption of drug compounds from molecular structure of Wessel is neither comparable nor analogous to the method of screening a compound library or portion thereof by absorption as claimed in the present

invention. For example, Applicants submit that Wessel fails to disclose or suggest at least the combination of the following features recited in amended claims 1 and 5, respectively.

> generating an *in vivo* absorption profile for each of said test samples from initial dose data and from the generated *in vitro* bioavailability data, wherein said *in vivo* absorption profile is characterized by one or more of rate of absorption, extent of absorption, and concentration of a test sample relative to a selected site of administration and a selected sampling site for one or more physiological barriers to absorption of a mammalian system of interest;
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> selecting a desired *in vivo* absorption profile;
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> screening said test samples from said primary compound library for *in vivo* absorption profiles that are above or equivalent to the desired *in vivo* absorption profile; and
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> generating a secondary compound library from said screening of said test samples;
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> generating a simulated *in* vivo absorption profile for each of said test samples from initial dose data and from *in vitro* bioavailability data, wherein said absorption profile is characterized by one or more of rate of absorption, extent of absorption, and concentration of a test sample relative to a selected site of administration and a selected sampling site for one or more physiological barriers to absorption of a mammalian system of interest, wherein said simulated *in vitro* absorption profile is generated by:
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> providing said initial dose data and said *in vitro* bioavailability data to a computer–implemented pharmacokinetic tool (PK tool) which comprises a s computer-readable components, an input/output system, a simulation engine, and a simulation model comprising a physiological model of said mammalian system of interest, wherein said input/output system, simulation engine and simulation model are capable of working together to carry out the steps of:

receiving through the input/output system as input data, said initial dose data and said *in vitro* bioavailability data for one or said test samples; and

generating as output data a simulated *in vivo* absorption profile for said test samples;

selecting a desired simulated *in* vivo absorption profile;

screening said test samples from said primary compound library for simulated *in vivo* absorption profiles that are above or equivalent to the desired simulated *in vivo* absorption profile; and

generating a secondary library from said screening of said test samples.

In fact, in characterizing the reference, the Examiner failed to sufficiently address, among others, the features of "providing a primary compound library..." and "a secondary compound library." Therefore, the Applicants submit that Wessel fails to disclose each and every element recited in amended claims 1 and 5 of the present application.

Moreover, to qualify as prior art under 35 U.S.C. §102, a single prior art reference must teach, i.e., identically describe, each feature of a rejected claim. As explained above, Wessel fails to disclose or suggest each and every feature of amended claims 1 and 5. Accordingly, the Applicants respectfully submit that amended claims 1 and 5 are not anticipated by Wessel. Therefore, the Applicants respectfully submit that claims 1 and 5 are allowable.

As claims 2, 3, 6-10, 12, 13, 15 and 16 depend from claims 1 or 5, respectively, the Applicants submit that each of these claims incorporates the patentable aspects

therein, and are therefore allowable for at least the reasons set forth above with respect to the independent claims, as well as for the additional subject matter recited therein.

Accordingly, the Applicants respectfully request withdrawal of the rejection.

**Conclusion**

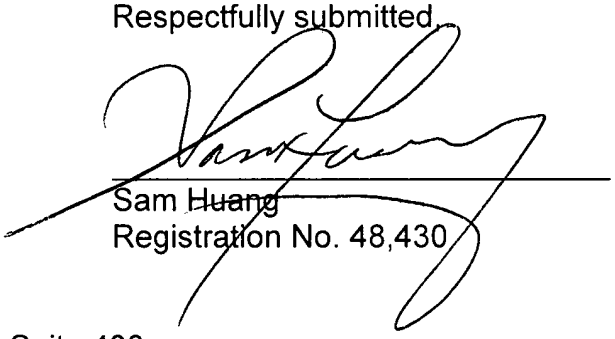
In view of the above, the Applicants respectfully submit that each of claims 1-17 recites subject matter that is neither disclosed nor suggested in the cited prior art. The Applicants also submit that the subject matter is more than sufficient to render the claims non-obvious to a person of ordinary skill in the art, and therefore respectfully request that claims 1-17 be found allowable and that this application be passed to issue.

If for any reason, the Examiner determines that the application is not now in condition for allowance, it is respectfully requested that the Examiner contact the Applicants' undersigned attorney at the indicated telephone number to arrange for an interview to expedite the disposition of this application.

In the event this paper has not been timely filed, the Applicants respectfully petition for an appropriate extension of time.

Any fees for such an extension, together with any additional fees that may be due with respect to this paper, may be charged to counsel's Deposit Account No. 01-2300, referring to client-matter number 109904-00028.

Respectfully submitted,



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